REMARKS/ARGUMENTS

With entry of the instant amendment, claims 1-56 and 58-72 are cancelled. Claim 57 is therefore under examination. Cancellation of subject matter is without prejudice for subsequent revival in a continuation application.

Claim 57 has been amended to recite inhibiting the growth of a human hairy-cell leukemia cell *in vivo* and to recite a recombinant immunoconjugate comprising a PE38 linked at its amino terminus to an RFB4 dsFv. Support for the amendment can be found throughout the application and claims, *e.g.*, in Fig. 2B and page 48.

Applicants thank the Examiner for the discussion on October 22, 2007 in which the current rejection and evidence of record was discussed.

Rejection under 35 U.S.C. § 103, obviousness

In the final Office Action of August 7, 2007, the Examiner maintained the rejection of claims 1-4, 7-11, 13, 14, 16, 17, 22-26, 29-32, 50-56, and 70-72 as allegedly obvious over the various references cited at page 2 of the Office Action. Although Applicants disagree for reasons of record, in the interests of expediting prosecution, claims 1-56 and 58-72 have been cancelled and claim 57 has been amended. To the extent that the Examiner would apply the rejection to amended claim 57, Applicants respectfully traverse.

Assuming *arguendo* that claim 57 could be considered *prima facie* obvious, the claim is additionally patentable due to the surprising results obtained using RFB4dsFV-PE38 in Phase I clinical trials for the treatment of hairy-cell leukemia. As previously explained (*see, e.g.*, Applicants' response filed May 7, 2007 and the article in *N. Engl. J. Med.* 345:241247, 2001, submitted with the May 7, 2007 response) in the Phase I clinical trials, eleven of sixteen patients achieved complete remission and two patients achieved partial remission when RFB4ds(Fv)-PE38 was administered to them. In the *N. Engl. J. Med.* article, the authors noted that they were unaware of any other treatment that can produce a high rate of complete remission in patients with hairy-cell leukemia that is resistant to purine analogues (*see,* p. 244, second column, the second to the last sentence of the first full paragraph). Applicants additionally submit herewith

an article dated Aug. 20, 2001 from the ACS News Center (attached as Appendix A) in which one of the inventors, Dr. Krietman, explains that while their team expected a successful trial based on laboratory testing, they were surprised at how good the results were and at how quickly, for most patients, complete remission was achieved (page 2, fourth paragraph of attached article).

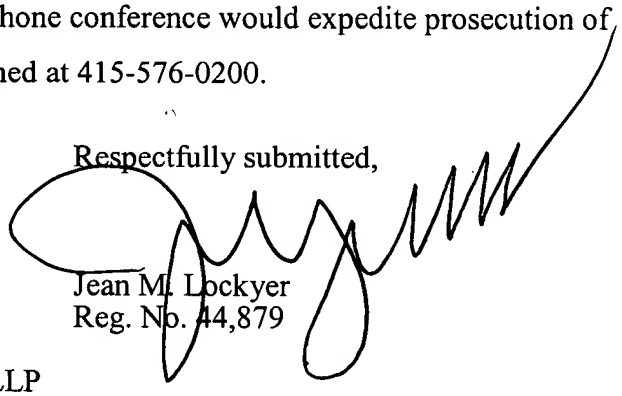
In view of the foregoing, claim 57 is patentable. Applicants therefore respectfully request withdrawal of the rejection.

CONCLUSION

Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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Appendix A

ACS News Center

Medical Updates XML

News You Can Use

Stories of Hope

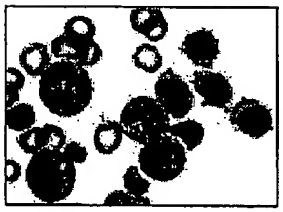
ACS Archives

ACS News Center Staff

New Drug Helps Hairy Cell Leukemia Patients

Treatment Follows Initial Therapy

Article date: 2001/08/20



While there is no special flag to guide conventional chemotherapy straight to cancer cells, researchers have designed a drug that specifically targets a type of leukemia. A recent article in the *New England Journal of Medicine* (Vol. 345, No. 4: 241-247) reports the drug is highly effective in hairy cell leukemia that has become resistant to conventional chemotherapy drugs.

Hairy cell leukemia, which has a fuzzy appearance of its cells under the microscope, is quite treatable, but not curable, according to Robert Kreitman, MD, chief of the clinical immunology section at the National Cancer Institute's laboratory of molecular biology, and one of the study authors.

Up to 85% of patients will achieve complete remission using standard therapy. But some will relapse after a number of years and will often be resistant to the same treatments that worked before. Once resistant, there's really no other effective treatment.

BL22 Fights Resistant Cancer

Researchers tested a drug called BL22 on 16 patients resistant to the standard hairy cell leukemia therapy. BL22 combines an antibody to target specific blood cells affected by the leukemia with a toxin to kill those cells. The average age of the patients was 54, and the average time from first diagnosis was eight years. All had received about three rounds of standard treatment and were pronounced resistant because they did not respond.

Of the patients enrolled in the study, 11 out of 16 went into complete remission, and two had partial responses. According to Kreitman, one of the partial responders has gone into complete remission since the study was published. The second patient is still being treated, with the goal to get him into complete remission, too.

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Of the three remaining patients in this phase I study, two were started on much lower doses of the drug. The main purpose of a phase I clinical trial is to find the best way to give a new treatment and how much of it can be given safely. Doctors conducting the trial will start by giving very low doses of the drug to the first patients and increasing the dose for later groups of patients until side effects appear.

The last patient was immune to the drug because he developed antibodies that destroyed it. So, of the 13 patients who got adequate treatment, all of them responded.

"As long as the patients aren't immune to the drug and they get a high-enough dose, we believe we can get complete remission in all patients," says Kreitman.

Kreitman adds that while his team had expected a successful trial based on laboratory testing, they were surprised at how good the results were. They were also surprised at how fast it all happened — most patients who achieved a complete remission did so after just one round of therapy.

Antibody Targeted Therapy is Restricted to Blood Cells

Unlike usual drugs that enter most cells throughout the body, BL22 is guided to cells that are flagged with a protein called CD22. This is a normal protein present on the surface of some types of normal blood cells, and on some forms of leukemia and lymphoma cells, but is not found elsewhere in the body.

By combining an antibody directed to this protein with a cellular poison, blood cells and leukemia cells marked with CD22 are destroyed. The antibody alone could find the leukemia cells, but couldn't kill them. The toxin alone would damage nearly all cells of the body and in high enough doses would be fatal.

Dawn Willis, PhD, MPH, director of research promotion and communication for the American Cancer Society, says an exciting aspect of this research is the use of a variety of antibodies and the hope that scientists may eventually be able to produce similar immunotoxin drugs that specifically target other forms of cancer.

"There's reason to believe that some of these targeted toxins are going to work. It's been an idea that's been around for at least 25 years," she says.

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